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Accompanying this Information Disclosure Statement is

- ☐ a statement as specified in 37 CFR 1.97(e); or
- ☒ the fee set forth in 37 CFR 1.17(p).

If fees are due, enclosed is our Check No. 10180 for \$180.00 in payment of the Information Disclosure Statement Fee. If it is determined that any additional fees are due, the Commissioner is hereby authorized to charge such fees to Deposit Account 500388 (Order No. MXGNP001X3).

Respectfully submitted,

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Form 1449 (Modified)	Atty Docket No. MXGNP001X3/124.610	Application No.: 09/618,579
Information Disclosure Statement By Applicant	Applicant: Selifonov et al.	
(Use Several Sheets if Necessary)	Filing Date July 18, 2000	Group 1643

U.S. Patent Documents

Examiner Initial	No.	Patent No.	Date	Patentee	Class	Sub-class	Filing Date
	A1	5,223,409	6/93	Ladner et al.			
	A2	5,198,346	3/93	Ladner et al.			
	A3	6,107,073	8/00	Chen			
	A4	5,741,691	4/21/98	Arnold et al.			
	A5	6,518,065	2/11/03	Stemmer			
	A6	6,365,408	4/2/02	Stemmer			
	A7	6,323,030	11/27/01	Stemmer			

Foreign Patent or Published Foreign Patent Application

Examiner Initial	No.	Document No.	Publication Date	Country or Patent Office	Class	Sub-class	Translation	
							Yes	No
/	B1	WO03/055978	10/7/03	WIPO			X	

Other Documents

Examiner Initial	No.	Author, Title, Date, Place (e.g. Journal) of Publication
✓	C1	Jan Drenth, Principles of Protein X-Ray Crystallography, Springer-Verlag, Pages 12-18, 1995
✓	C2	Robert F. Service, "Tapping DNA for Structures Produces a Trickle," News Focus, Science, Vol. 298, Pages 948-950, 2002
✓	C3	Accelrys Website, GCG Wisconsin Package, 15 Pages, 2002
✓	C4	Lewis Ricki, The Scientist, Pages 1-4, 1993
✓	C5	Chen et al., "Tuning the Activity of an Enzyme for Unusual Environments: Sequential Random Mutagenesis of Subtilisin E for Catalysis in Dimethylformamide," Proc. Natl. Acad. Sci. USA, Vol. 90, Pages 5618-5622, 1993
✓	C6	Abkevich et al., "Impact of Local and Non-Local Interactions on Thermodynamics and Kinetics of Protein Folding," J. Mol. Biol., 252: 460-471, 1995
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/	C8	M. Ostwemeier et al., "A Combinatorial Approach to Hybrid Enzymes Independent of DNA Homology," <i>Nature Biotechnology</i> , Vol. 17, pp. 1205-1209, 1999
/	C9	Arnold, "Combinatorial and Computational Challenges for Biocatalyst design", <i>Nature</i> , 2001, 409(6817):253-257
/	C10	Boder et al., "Directed Evolution of Antibody Fragments with Monovalent Femtomolar Antigen binding Affinity", <i>Proc. Natl. Acad. Sci. USA</i> , 2000 97 (20):10701-10705
/	C11	Bohm, "New approaches in molecular structure prediction", <i>Biophys Chem.</i> , 1996, 59: 1-32
/	C12	Chen & Arnold, F.H., "Tuning the Activity of an Enzyme for Unusual Environments: Sequential Random Mutagenesis of Subtilisin E for Catalysis in Dimethyiformamide", <i>Proc. Natl. Acad. Sci. U.S.A.</i> 1993, 90:5618-5622
/	C13	De Maeyer et al., "All in One: A Highly Detailed Roamer Library Improves Both Accuracy and Speed in the Modeling of Sidechains by Dead-End Elimination", <i>Folding & Design</i> , 1997, 2, 53-66
/	C14	Desjarlais & Clarke N.D., "Computer Search Algorithms in Protein Modification and Design," <i>Curr. Opin. Struct. Biol.</i> , 1998, 8:471-475
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/	C16	Dunbrack & Karplus, M., "Backbone-Dependent Rotamer Library for Proteins Application to Sidechain Prediction," <i>J. Mol. Biol.</i> 1993, 230:543-574
/	C17	Dunbrack & Karplus, "Conformational Analysis of the Backbone-Dependent Roamer Preferences of Protein Sidechains," <i>Nature Struct. Biol.</i> 1994, 1:334-340
/	C18	Fetrow et al., "New program for Protein Tertiary Structure Prediction," <i>Biotechnol.</i> , 1993, 11(4):479-484
/	C19	Flickinger et al., "Enzymes, Directed Evolution", in 2 <i>Encyclopedia of Bioprocess Technology: Fermentation, Biocatalysis, and Bioseparation</i> 1999, 2:971-987
/	C20	Giver et al, "Directed evolution of a Thermostable Esterase," <i>Proc. Natl. Acad. Sci., USA</i> 1998, 95:12809-12813
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✓	C22	Hogue et al., "Structure Databases," <i>Methods Biochem. Anal.</i> 1998, 39:46-73
✓	C23	Johnson et al., "The Traveling Salesman Problem: A Case Study in Local Optimization," In <i>Local Search in Combinatorial Optimization</i> , Edited by Aarts et al., John Wiley & Sons Ltd., 21-310, 1997
✓	C24	Geladi et al., "Partial Least Squares Regression: A Tutorial," <i>Anal Chim Acta</i> , 168: 1-17, 1986
✓	C25	Holowachuk et al., "Efficient Gene Synthesis by Klenow Assembly/Extension-Pfu Polymerase Amplification (KAPPA) of Overlapping Oligonucleotides," <i>PCR Methods Appl</i> , 4:299-302, 1995
✓	C26	Aita et al., "Theory of Evolutionary Molecular Engineering Through Simultaneous Accumulation of Advantageous Mutations," <i>J. Theor. Biol.</i> , 207:543-556, 2000
✓	C27	Jain et al., "The Crystal Structure of an Autoprocessed Ser221 Cys-subtilisin E-propeptide Complex at 2.0 Å Resolution," <i>Mol. Biol.</i> 1998, 284:137-144
✓	C28	Joo et al., "Laboratory Evolution of Peroxide-Mediated Cytochrome P450 Hydroxylation," <i>Nature</i> 1999, 399:670-672
✓	C29	Kay, "NMR Methods for the Study of Protein Structure and Dynamics," <i>Biochem. Cell Biol.</i> , 1997, 75:1-15 (1997)
✓	C30	Koehl & Delarue, "Application of a Self-consistent Mean Field Theory to Predict Protein Side-chains Conformation and Estimate Their Conformational Entropy," <i>J. Mol. Biol.</i> 1994, 239:249-275
✓	C31	Koehl & Delarue, "Mean-field Minimization Methods for Biological Macromolecules," <i>Curr. Opin. In Struct. Biol.</i> 1996, 6:222-226
✓	C32	Lazar, "De Novo Design of the Hydrophobic Core of Ubiquitin," <i>Protein Science</i> , 1997, 6: 1167-1178
✓	C33	Lee & Richards, "The Interpretation of Protein Structures: Estimation of Static Accessibility," <i>J. Mol. Biol.</i> , 1971, 55: 379-400
✓	C34	Lee & Subbiah, "Prediction of Protein Side-chain Conformation by Packing Optimization," <i>J. Mol. Biol.</i> , 1991, 217:373-388
✓	C35	Lee, "Predicting Protein Mutant Energetics by Self-consistent Ensemble Optimization," <i>J. Mol. Biol.</i> , 1994, 236:918-939
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	C51	You & Arnold, "Directed Evolution of Subtilisin E in <i>Bacillus Subtilis</i> to Enhance Total Activity in Aqueous Dimethylformamide", <i>Protein Engineering</i> 1994, 9(1):77-83
✓	C52	Zhao & Arnold, "Optimization of DNA shuffling for High Fidelity Recombination," <i>Nuci. Acids Res.</i> , 1997, 25(6):1307-1308
	C53	Zhao & Arnold, "Directed Evolution Converts Subtilisin E into a Functional Equivalent of Thermitase," <i>Protein Engineering</i> 1999, 12(1):47-53
	C54	Martin et al., "Measuring Diversity: Experimental Design of Combinatorial Libraries for Drug Discovery," <i>J. Med. Chem.</i> 38, 1431-1436, 1995
	C55	Sheridan et al., "Using a Genetic Algorithm to Suggest Combinatorial Libraries," <i>J. Chem. Inf. Compu. Sci.</i> , 35, 310-320, 1995
	C56	D.K. Agrafiotis, "Multiobjective Optimization of Combinatorial Libraries," <i>IBM J. Res & Dev.</i> , Vol, 45, No. 3, 545-566, 2001
	C57	Peter Halling, "Is Random Mutation More Rational", <i>Nature Biotechnology</i> , Vol. 14, April 1996
	C58	Jonathan King, "Unexpected Pathways to Protein Stabilization", <i>Nature Biotechnology</i> , Vol. 14, April 1996
	C59	Roger Sheldon, "Picking a Winner", <i>Nature</i> , vol. 399, June 17, 1999, pp. 636-637
	C60	Holler et al., "In Vitro evolution of a T Cell Receptor with High Affinity for Peptide /MHC", <i>Proc. National Academy Sci USA</i> , Vol, 97, No. 10, May 9, 2000, pp. 5387-5392
	C61	Foote et al., "Breaking the Affinity Ceiling for Antibodies and T. Cell Receptors, <i>Proc. National Academy Sci USA</i> , Vol. 97, No. 20, September 26, 2000, pp. 10679-10681
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✓	C36	Levitt et al., "Protein folding: The endgame," <i>Annu. Rev. Biochem.</i> , 1997, 66:549-579
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✓	C38	Matsumura et al., "Structural Studies of Mutants of T4 Lysozyme That Alter Hydrophobic Stabilization," <i>J. Biol. Chem.</i> 1989, 264:16059-16066
✓	C39	Miyazaki & Arnold, "Exploring Nonnatural Evolutionary Pathways by Saturation Mutagenesis: Rapid Improvement of Protein Function," <i>J. Molecular Evolution</i> , 1999, 49:716-720
✓	C40	Miyazaki & Arnold, "Directed Evolution Study of Temperature Adaptation in a Psychrophilic Enzyme," <i>J. Mol. Biol.</i> 2000, 297:1015-1026
✓	C41	Moore & Arnold, "Directed Evolution of a Para-nitrobenzyl esterase for aqueous-organic Solvents," <i>Nature Biotechnology</i> , 1996, 14(4):458
✓	C42	Nikolova et al., "Semirational Design of Active Tumor Suppressor P53 DNA Binding Domain with Enhanced Stability," <i>Proc. Natl. Acad. Sci. U.S.A.</i> 1998, 95:14675-14680
✓	C43	Pjura et al, "Development of an <i>in vivo</i> Method to Identify Mutants of Phage T4 lysozyme of Enhanced Thermostability," <i>Protein Science</i> 1993, 2:2217-2225
✓	C44	Fontana & Shuster, "Continuity in Evolution: On the Nature of Transitions," <i>Science</i> 1998, 280:1451-1455
✓	C45	Sasai, "Conformation, Energy, and Folding Ability of Selected Amino Acid Sequences," <i>Proc. Natl. Acad. Sci. USA</i> , 1995, 92: 8438-8442
✓	C46	Saven & Wolynes, "Statistical Mechanics of the Combinatorial Synthesis and Analysis of Folding Macromolecules," <i>J. Phys. Chem. B</i> 1997, 101:8375-8389
✓	C47	Skandalis <i>et al.</i> , "Creating Novel Enzymes by Applied Molecular Evolution," <i>Chem. Biol.</i> 1997, 4:889-898
✓	C48	Whitlow, "1.85 Å structure of Anti-Fluorescein 4-4-20 Fab," <i>Protein Engineering</i> , 1995, 8:749-761
✓	C49	Wilson et al., "Modeling Side-chain Conformation for Homologous Proteins Using an Energy-Based Rotamer Search," <i>J. Mol. Biol.</i> 1993, 229:996-1006.
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